Effect of Gaseous Media on the Balance Between Cardiac Outputs of the Right and Left Ventricles

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 132, No. 11, pp. 514-518, November, 2001
Original article submitted July 2, 2001

Acute experiments on cats showed that mild hypoxia did not disturb the balance between right and left ventricular outputs. Breaching 3% O_2 shifted this balance by reducing right ventricular output in cats with low resistance to hypoxia. Spontaneous breathing hypercapnic gas mixtures shifted this balance towards the left ventricular output. During artificial ventilation under open chest conditions, hypercapnia induced opposite changes and shifted the balance towards the right ventricular output.

Key Words: *balance between the left and right ventricular output*; *hypoxia*; *hypercapnia*; *ultrasound methods*

Despite considerable functional and structural differences between the left (LV) and right ventricles (RV) they normally eject equal amounts of blood. If this equilibrium is disturbed, it must be restored as soon as possible, because long-term imbalance between the left and right hearts is life threatening [2,3,11,12]. In our previous experiments we demonstrated that damage to the pulmonary vascular bed during toxic pulmonary edema leads to redistribution of blood to the pulmonary circulation (RV output exceeds LV output) [5]. By contrast, pulmonary artery occlusion resulting from fat embolism is associated with reduced total cardiac output and significant imbalance between LV and RV outputs (redistribution of the blood to the pulmonary circulation) [4].

Here we studied the effects of hypoxia, hypercapnia, and some vasoactive agents such as epinephrine, norepinephrine, or histamine on the balance between LV and RV outputs.

MATERIALS AND METHODS

Experiments were carried out on 28 male and female cats (2.8-4.5 kg) anesthetized with Nembutal (40 mg/kg, intraperitoneally). In 18 closed chest spontaneously breathed cats RV and LV outputs were measured by ultrasound technique [1]. Ultrasound cuff probes calibrated in volumetric flow units were positioned on the ascending aorta and pulmonary artery cone. The recorded parameters were fed to an analog device and the ratio between mean flows in the ascending aorta and pulmonary artery cone was calculated on-line. In our analysis we assumed that blood flow in the pulmonary artery cone (or RV output) is an adequate estimate of venous return to the heart. In experiments with artificial ventilation the probes were positioned on the corresponding vessels, the chest was closed layer-by-layer, and the animals were switched to spontaneous breathing. Blood pressure was measured in the femoral and pulmonary arteries. Chest excursions were recorded with a strain gage. The effects of negative thoracic pressure [7,13] on RV and LV outputs were studied on 10 artificially ventilated open-chest cats.

The effects of normobaric hypoxia and hypercapnia on cardiac function were studied on cats breathing various hypoxic and hypercapnic gas mixtures for 5-10 min. Hypoxic mixtures contained nitrogen and 10, 7.5, 5, or 3% O_2. Hypercapnic mixtures contained 5, 7, or 10% CO_2. Breathing 3% O_2 was continued until apnoe and the animals were divided into low (1-3 min), moderate (4-8 min), and highly resistant to hypoxia (more than 9 min) [6].

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0007-4888/01/1325-1051$25.00

We also studied the effects of epinephrine (5-10 μg/kg), norepinephrine (1-2 μg /kg), and histamine (2-5 μg /kg) on cardiac output.

RESULTS

Mild hypoxia (10% O_2) caused no changes in cardiac output in spontaneously breathing cats. Breathing 7.5% and 5% O_2 increased both LV and RV outputs by 15-20% and usually did not impair the balance between these parameters. However, in some experiments breathing 5% O_2 was accompanied by impalance between LV and RV outputs: aortal blood flow remained unchanged, while pulmonary blood flow after 2-3 min decreased by 10-15%. The balance recovered after resumption of air ventilation. Strong hypoxia (3% O_2) caused different responses in cats with different resistance to hypoxia. In highly resistant animals cardiac output increased by 20-30% without imbalance between LV and RV outputs. However, resumption of breathing after apnea and switching to air ventilation was accompanied by more rapid recovery of aortic blood flow compared to that in the pulmonary artery, *i.e.* redistribution of the blood into systemic circulation. By 2 to 3 min later, the balance between LV and RV outputs recovered (Fig. 1, *a*).

In some animals with moderate resistance to hypoxia, pulmonary blood flow increased, while aortic flow remained unchanged, or slightly decreased during strong hypoxia. This imbalance between LV and RV outputs suggests an increase in venous return and, probably, blood deposition in the lungs [7,8].

In animals with low resistance to hypoxia, breathing 3% O_2 led to imbalance between LV and RV outputs. Blood flow in the pulmonary artery considerably decreased against the background of unchanged or slightly decreased blood flow in the ascending aorta, which implies a decrease in venous return (Fig. 1, *b*). In these animals severe hypoxia was accompanied by a drop of blood pressure. Published data suggest that changes in the blood flow in caval veins reflect changes in systemic blood pressure. [7]. A transient increase in LV output can be due to reserve LV volume [2,10,14] and blood deposed in the lungs [7,8].

It is likely that activation of the sympathoadrenal control underlies the circulatory responses to a strong hypoxic stimulus in highly resistant animals. By contrast, the prevalence of parasympathetic control in low resistant animals leads to a circulatory hypofunction [9]. In particular, this leads to a reduction of systemic blood pressure and imbalance between LV and RV function.

It can be hypothesized that imbalance between LV and RV outputs is the main cause of death in low and moderate resistant animals. In highly resistant animals, hypocapnia is an important factor, which together with hypoxia leads to respiratory arrest, as hemodynamic parameters remained high until apnoe [6].

In open chest animals, hypoxia during artificial ventilation caused less prominent changes in cardiac output than during spontaneous breathing. In some experiments, no changes were observed. The balance between LV and RV outputs was usually preserved.

In spontaneously breathing animals, hypercapnia induced opposite changes in LV and RV outputs. Du-

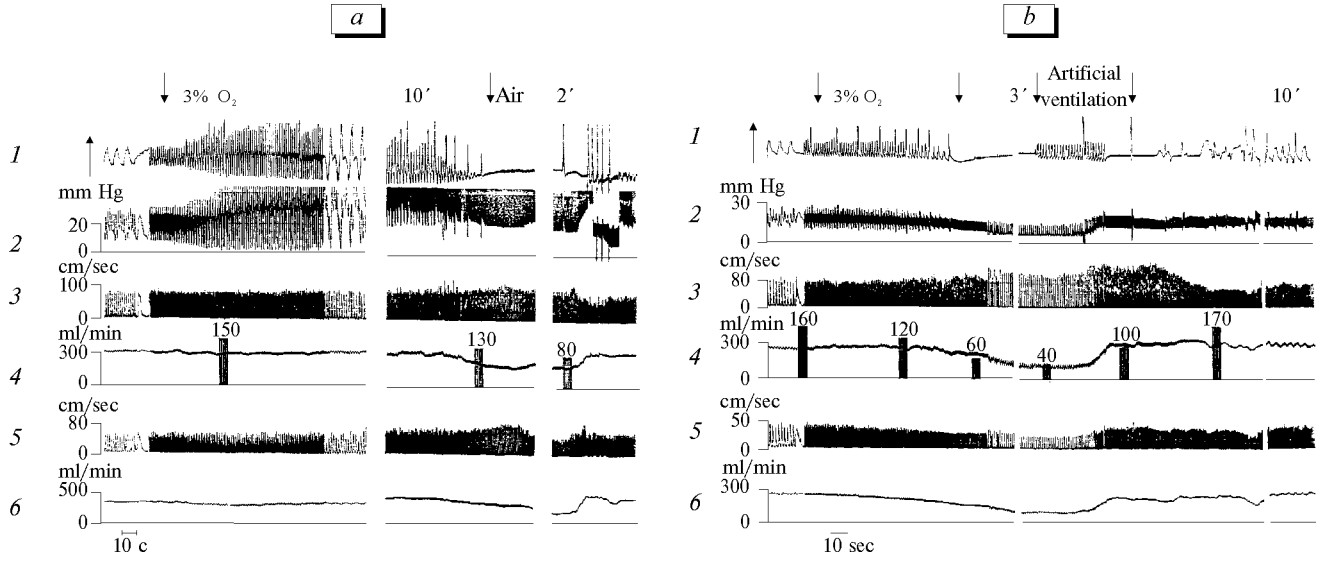

Fig. 1. Changes in hemodynamics and respiration in cats with high (*a*) and low (*b*) resistance to hypoxia during breathing hypoxic mixture containing 3% O_2. *1*) Respiration (upward arrow indicates inspiration); *2*) blood pressure in the pulmonary artery; *3*) linear blood flow velocity in the ascending aorta; *4*) blood flow rate in the ascending aorta; *5*) blood flow velocity in the pulmonary artery; *6*) blood flow rate in the pulmonary artery. Bars: blood pressure in the femoral artery. Here and on Fig. 2: bottom lines on each curve show zero levels; numbers at the top are stimulation or recovery timing marks. Arrows indicate start and end of gas mixture breathing.

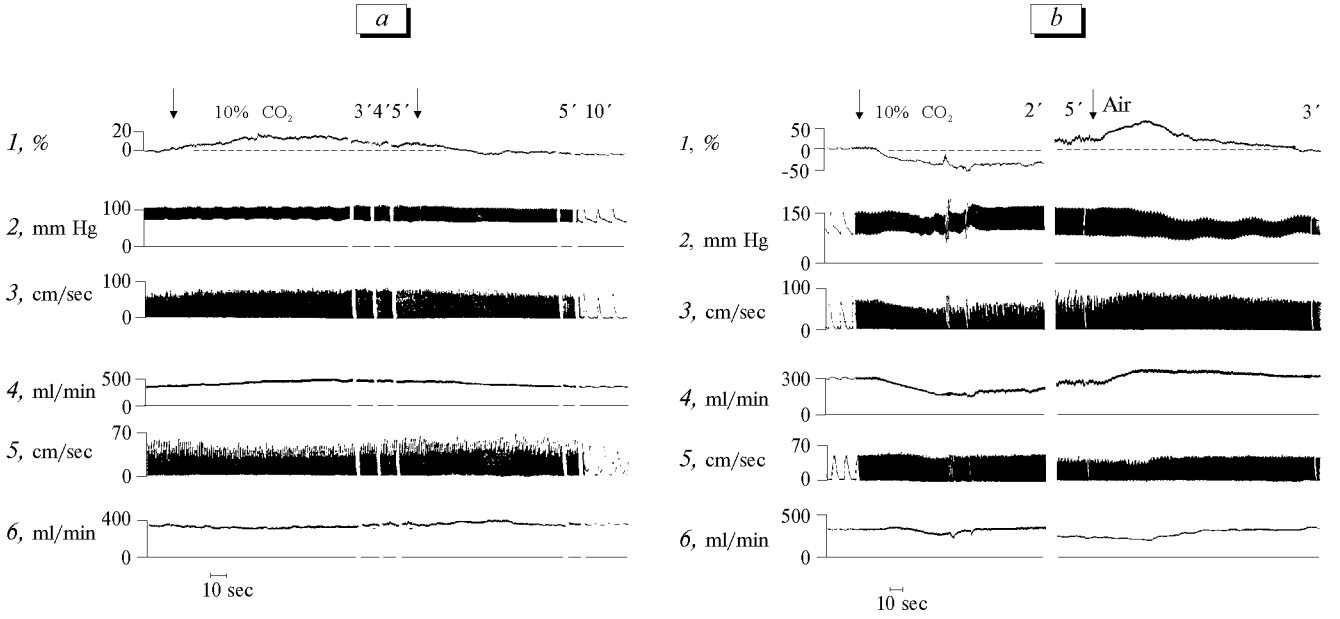

Fig. 2. Changes in hemodynamics during spontaneous breathing hypoxic mixture containing 10% O_2 (*a*) and under artificial ventilation in open-chest cats (*b*). Here and on Fig. 3: *1*) balance between right and left ventricular outputs: positive changes on the curve correspond to a relative increase in ascending aortic flow compared to the flow in the pulmonary artery cone, and, vice versa, negative changes correspond to a relative increase in pulmonary flow compared to aortic flow; *2*) blood pressure in the femoral artery; *3*) linear blood flow velocity in the ascending aorta; *4*) volume blood flow rate in the ascending aorta; *5*) linear blood flow velocity in the pulmonary artery cone; *6*) volume blood flow rate in the pulmonary artery.

ring first few minutes of stimulation, blood flow in the ascending aorta increased by 30-40%, while in the pulmonary cone it decreased by 10-15%, or remained at the initial level, suggesting unchanged or decreased venous return and, probably, mobilization of the blood deposed in the lungs [7,8]. The pulmonary flow increased 2.5-3 min after the start of stimulation, while the aortic flow decreased, and the balance recovered. This tendency was observed in animals breathing 5% CO_2, and in animals breathing 10% CO_2 these changes became clearly seen (Fig. 2, *a*).

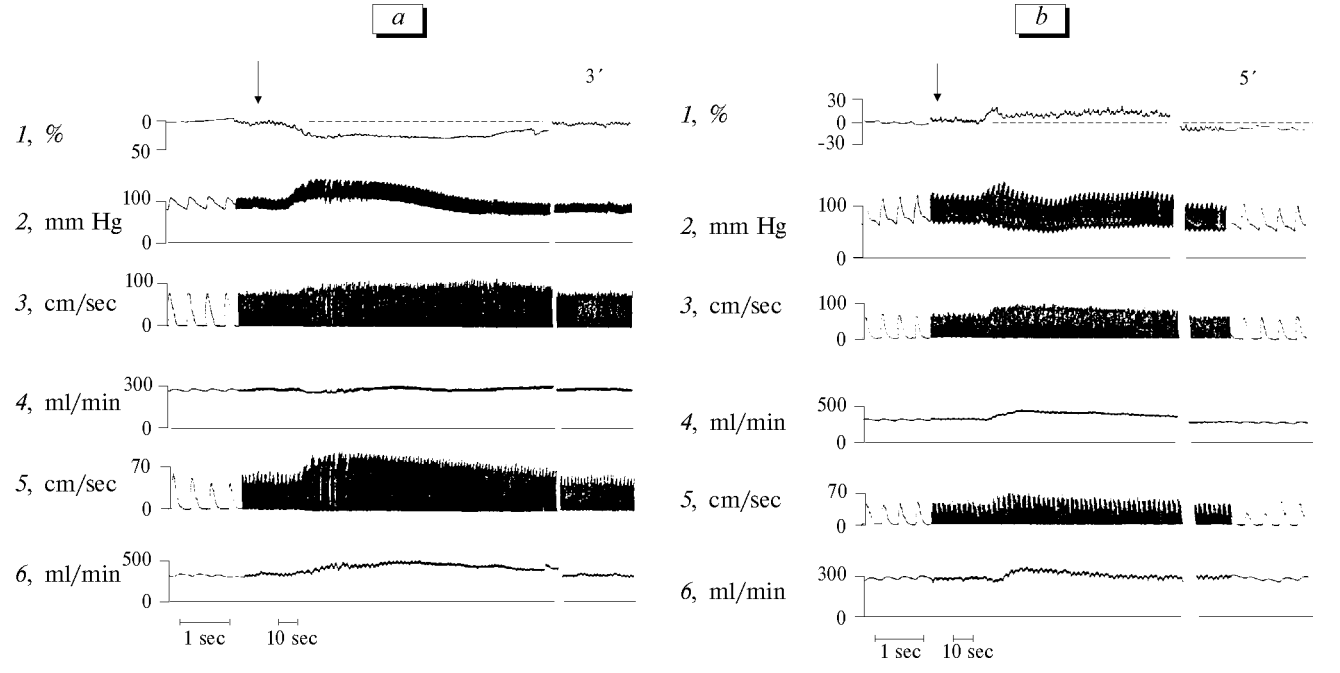

Fig. 3. Changes in hemodynamics during intravenous injection of epinephrine (10 μg) in spontaneously breathing cats (*a*) and in open-chest artificially ventilated cats (*b*). Arrows indicate start and end of epinephrine infusion.

During artificial ventilation, the shifts in RV and LV outputs were opposite to those observed during spontaneous breathing: aortic flow decreased by 30-40%, while pulmonary flow remained unchanged or slightly increased. Blood redistribution to the pulmonary circulation started on the 10th-20th sec of hypercapnia and continued for 2.5-3 min. Then, the flow in the ascending aorta increased (probably due to blood mobilization from the lungs), and the flow in the pulmonary artery decreased, which restored the balance between LV and RV outputs (Fig. 2, *b*).

One could suppose that hypercapnia would change venous return differently in spontaneously breathing and artificially ventilated open-chest animals. However, experiments revealed that RV output was relatively stable in both cases. Thus, the imbalance between the two hearts was caused by changes in LV output, which in turn were determined by hemodynamics changes in the pulmonary circulation [8].

During asphyxia (tracheal occlusion or artificial ventilation switching off) characterized by hypoxia in combination with hypercapnia, LV output surpassed RV output both under open chest and closed chest conditions. This was observed immediately after the onset of asphyxia (1.5-2.0 min), when cardiac output persisted at a relatively high level, and after its decrease: the decrease in LV output was preceded by the decrease in RV output.

In spontaneously breathing animals, intravenous injections of epinephrine, norepinephrine, or histamine increased RV output by 30-50%, while aortic flow remained unchanged or insignificantly increased (by 15-20%). Such imbalance between LV and RV outputs was characterized by prevalence of RV output irrespective of changes in systemic BP. The pulmonary flow increased 10-20 sec after injection of preparation, remained at a higher level for 1.5-2.0 min, and then gradually decreased. Aortic flow gradually increased and after 3 min the balance between RV and LV outputs recovered (Fig. 3, *a*).

In most artificially ventilated open-chest cats, blood flows in the pulmonary cone and ascending aorta synchronously increased after intravenous injection of test preparations with a slight prevalence of aortic flow (Fig. 3, *b*). In some experiments, aortic flow increased, while pulmonary flow remained unchanged.

Thus, intravenous injection of epinephrine, norepinephrine, or histamine induces opposite shifts in the balance between RV and LV outputs during spontaneous breathing and during artificial ventilation under open chest conditions. It can be concluded that stability or instability of the balance resulted from diverse shifts in the peripheral and pulmonary circulation induced by different stimuli.

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